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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,761	02/21/2006	Takamasa Watanabe	0020-5502PUS1	6669

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
06/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/568,761	WATANABE ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,20,31 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-20 and 31-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 5/2/08, is acknowledged.

2. Claims 19-20 and 31-32 are pending are pending and under examination as they read on a method for improving or treating of inflammatory bowel disease (IBD), comprising administering a therapeutic agent comprising an effective amount of anti-CD81 antiody to a mammal in need thereof.

3. The following new ground of rejections are necessitated by the amendment submitted 5/2/08.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 19-20 and 31-32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The term "biological activity of CD81" in claim 19 is indefinite. It is not clear what CD81 biological activity is encompassed in the claim.

B. The recitation "in which the administration of anti-CD81 antibody is associated with lengthening of the colon of said mammal" in claim 32 is ambiguous. It is not clear what is encompassed by the claims. It is not clear whether the antibody causes "the lengthening of the colon" or treat IBD associated with "the lengthening of the colon".

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 19-20 and 31-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a method of improving or treating IBD comprising administering the anti-CD81 monoclonal antibody 2F7 (once the deposit is satisfied).

Applicant is not in possession of any "anti-CD-81 antibody which blocks a biological activity of CD81" that would treat IBD (Applicant's attention is directed to examples 10 and 11 of the Written Discription). The US 20020192748 teaches that using three separate antibodies, 2F7, Eat1, and Eat2, which recognize *unique epitopes in the extracellular domains* of the CD81

protein, we show that there is a unique domain, recognized by Eat1, that is required for astrocyte cell-cycle withdrawal in response to neurons. This is likely due to conformational changes in the CD81 molecule, as inclusion of 2F7 actually augments neuron-induced astrocyte growth arrest (see 443¶).

Applicant has disclosed only 2F7 antibody; therefore, the skilled artisan cannot envision all the contemplated antibody possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 19-20 and newly added claim 32 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S Pat. No. 6,423,501.

The `501 patent teaches a method of treating inflammatory condition in a mammal comprising administering to the mammal an effective amount of an agent which induces CD81-mediated signal transduction. For example, the method can be used to treat inflammatory responses

associated with disorders such inflammatory bowel disease (i.e., Crohn's disease and ulcerative colitis) (see col., 13, lines 34-45 in particular). The `501 patent teaches that agents described herein can be anything which binds to or interacts with CD81 and induces (i.e., activates) or enhances CD81-mediated signal transduction. For example, the agent can be a polyclonal or monoclonal antibody, such as an anti-CD81 antibody. In particular embodiments, the antibody is 5D1 or 1A12 (see col., 9, line 65 to col., 10, line 3 in particular). The `501 patent further teaches that injections of anti-CD81 yielded significant inhibition of PCA reactions (blocks a biological activity of CD81) (see FIG. 10B). The functional properties claimed in claim 32 are inherent.

The reference teachings anticipate the claimed invention.

10. Claims 19-20 and newly added claim 32 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/25647 (IDS ref. No. BJ).

The `647 publication teaches a method of treating inflammatory condition in a mammal comprising administering to the mammal an effective amount of an agent which induces CD81-mediated signal transduction. For example, the method can be used to treat inflammatory responses associated with disorders such inflammatory bowel disease (i.e., Crohn's disease and ulcerative colitis) (see col., 26, lines 12-22 in particular). The `501 patent teaches that agents described herein can be anything which binds to or interacts with CD81 and induces (i.e., activates) or enhances CD81-mediated signal transduction. For example, the agent can be a polyclonal or monoclonal antibody, such as an anti-CD81 antibody. In particular embodiments, the antibody is 5D1 or 1A12 (see Pg. 19, line 3-9 in particular). The `647 publication further teaches that injections of anti-CD81 yielded significant inhibition of PCA reactions (blocks a biological activity of CD81) (see FIG. 10B). The functional properties claimed in claim 32 are inherent.

The reference teachings anticipate the claimed invention.

Applicant's arguments, filed 5/2/08, have been fully considered, but have not been found convincing.

Applicant submits that the claims are distinguishable from the teachings of the cited references. In particular, the claims recite that the anti-CD81 antibody is one that blocks a biological activity of CD81". Applicant further submits that the cited references teach that agents for treating IBD can be anything which binds to or interacts with CDS1 and induces (i.e. activates) or enhances CD81-mediated signal transduction. The anti-CD81 antibody which can be used in US '501 or WO '647 patent must activate or enhance a biological effect of CDS1, and therefore are different from the antibody recited in claim 19. Indeed, the cited references teach away from the instant invention, which reflects that inhibiting a biological activity of CD-81 provides a therapy for treatment of IBD

In contras to Applicant assertions, The Examiner notes that both the patent and the publication teach that injections of anti-CD81 yielded significant inhibition of PCA reactions (blocks a biological activity of CD81) (see FIG. 10B).

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 19-20 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S Pat. No. 6,423,501 or WO 98/25647 each Boismenu et al and Owens *et al* (1994).

The teachings of Pat. No. 6,423,501 or WO 98/25647 publication have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of anti-CD-81 antibody which blocks a biological activity of CD81 in claim 19 and fab, F(ab`)2 or Fv or scFv in claim 31.

Boismenu et al teach the identification of the TM4 protein CD81 as the ligand for mAb 2F7 (27). Monoclonal antibody 2F7 precipitates a unique 25-kD protein at the cell surface of PAM cells. The 25-kD protein recognized by mAb 2F7 could be purified after large-scale immunoprecipitation, as evaluated by SDS-PAGE and silver stain. Sequence analysis of a tryptic peptide from the 25-kD protein yielded the sequence FYDQALQQAVMDDDANNA (mouse CD81 residues 125 to 143) (see Fig 2 in particular). Boismenu et al further identified one mAb (2F7) that abrogated the appearance of CD4+CD8+ thymocytes bearing TCRct in fetal thymus organ cultures (FTOCs) (see page 198, 1st col.).

Owens *et al* teach the modification of murine antibodies such as a single chain antibody, a Fab fragment, a $F(ab')_2$ fragment. Owens *et al* further teach that antibody fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement –dependent cytotoxcity (see the entire document).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute the anti–CD81 antibody taught by 6,423,501 or WO 98/25647 the 2F7 monoclonal antibody taught by Boismenu et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because 2F7 is specific for CD81 that abrogated the appearance of CD4+CD8+ thymocytes bearing TCRct in fetal thymus organ cultures (FTOCs) as taught by Boismenu et al.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to produce the monoclonal antibody taught by 6,423,501 or WO 98/25647 a Fab and $F(ab')_2$ fragments taught by the Owens *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al.*

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be

left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

June 8, 2008

/Maher M. Haddad/
Primary Examiner,
Art Unit 1644